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EFFICACY AND SAFETY OF ROSUVASTATIN VERSUS ATORVASTATIN IN DYSLIPIDEMIA PATIENTS: A COMPARATIVE, OPEN LABEL PROSPECTIVE STUDY

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ABSTRACT

The objective of the study was to evaluate the efficacy and safety of the new statin, rosuvastatin compared with the established statin, atorvastatin. This open-label, randomized, parallel group, comparative, prospective study of 12-weeks duration included 40 patients with dyslipidemia divided into two groups of 20 each. Group-1 patients have received tablet rosuvastatin 10 mg once daily and group-2 received tablet atorvastatin 10 mg once daily for 12 weeks each. The levels of serum cholesterol, serum triglyceride, LDL, VLDL, and HDL were assessed at baseline and at the end of 12 weeks along with all the basic biochemical tests including ALT and CK-MB. The LDL level reduction in rosuvastatin group statistically nonsignificant when compared with atorvastatin group but the rise in HDL levels in rosuvastatin group after therapy was statistically significant when compared with atorvastatin group. 10 mg of rosuvastatin was comparable to 10 mg of atorvastatin in reducing LDL levels but more efficacious than 10 mg rosuvastatin in increasing HDL levels after 12 weeks of therapy in patients with dyslipidemia.

Keywords: Atorvastatin, Dyslipidemia, Rosuvastatin, Lipid Profile

INTRODUCTION

Cardiovascular diseases (CVD) are the most prevalent cause of death and disability in both developed as well as developing countries **[1]**. South Asians around the globe have the highest rates of Coronary Artery Disease (CAD) **[2]**. According to National Commission on Macroeconomics and Health (NCMH), a government of India undertaking,

there would be around 62 million patients with CAD by 2015 in India and of these, 23 million would be patients younger than 40 years of age **[3].** CAD is usually due to atherosclerosis of large and medium sized arteries and Dyslipidemia has been found to be one of the most important contributing factor **[4].** The value of treating various dyslipidemias with 3-hydroxy-3-methylglutaryl-coenzyme A reductase inhibitors (statins) for preventing major cardiovascular events and stroke has been well documented **[5-8].** As such, statins have become the keystone of therapy in the treatment of dyslipidemia for both the primary and secondary prevention of cardiovascular disease **[9, 10].** Rosuvastatin, a new member of statin group, has been shown to reduce LDL-C in a dose-dependent fashion by 46% to 55%, and has a similar safety profile to other statins **[11].** Compared with other statins, however, the terminal half-life of rosuvastatin is relatively long at approximately 18 h to 20 h **[12].**The present study was thus planned to primarily evaluate and then to compare the efficacy and safety of newer emerging and promising statin rosuvastatin *vs* existing commonly used statin such as atorvastatin in patients with dyslipidemia in Indian population.

MATERIALS AND METHODS

This study was open-label, randomized, parallel group, comparative, prospective study in patients with dyslipidemia. A total of Forty patients of dyslipidemia were included in the study after taking written informed consent. They were divided into two groups of 20 each.

Inclusion Criteria

Both male (35 - 55 years) and female patients (45 - 65 years) having low density lipoprotein cholesterol (LDL-C) higher than 130 mg/dl and triglycerides (TG) more than 240 mg/dl were included in the study.

Exclusion Criteria

The exclusion criteria for patients were clinically significant deviation from normal in physical examination, laboratory parameters, ECG, or chest X-ray. Clinically significant cardiovascular disease, including a history of congestive heart failure, angina pectoris within 1 year and history of myocardial infarction within 1 year, convulsive disorder, clinically significant gastrointestinal disease, including active peptic ulcers within the preceding 5 years, renal disease, hepatic disease, hematologic disease and insulin-dependent diabetes mellitus, and known infection with human immunodeficiency virus, were excluded. Subjects with the presence of any acute illness, h/o sensitivity

to statins, history of any musculo-skeletal disorder, history of alcohol, barbiturate, marijuana, or multidrug abuse, participation in other investigational drug studies within 30 days before the start of the study, subjects who are unlikely to be compliant with the protocol requirements, pregnant or lactating females, patients with history of use of any of the statins for at least 6 months prior to the commencement of the study and smokers were also excluded.

Study Visits and Treatment Schedule

Approval of the ethical committee of Rajiv Gandhi Institute ofMedical Sciences, Kadapa was taken prior to the start of the study. Included patients were explained in detail about the study protocol and related hazards. Those included underwent all baseline investigations such as liver function tests, kidney function tests, blood sugar level, fundoscopy, and baseline lipid profile, which was repeated at the end of the study. Enrolled patients were divided into two groups of thirty each by computer generated randomization chart (calculated from True Epistat, Standard version 1999). Group-1 patients received rosuvastatin10 mg tablet once daily and group-2 received atorvastatin tablet 10mg once daily for a period of 12 weeks. All patients were given advice about diet and exercise.

Statistical Analysis

The statistical calculation for the paired t-test, unpaired t-test and Fischer exact test were performed with statistical software Instat+ version 3.036 (Statistical Services Center, University of Reading, UK). $P < 0.05$ is considered statistically significant and $P < 0.001$ is considered highly statistically significant.

RESULTS

Both rosuvastatin and atorvastatin were very effective in reducing the levels of serum cholesterol, serum triglyceride, LDL, and VLDL after treatment for 12 weeks in patients with dyslipidemia. The reductions in these lipid parameters were highly significant. Both the statins also increased the levels of HDL significantly ($P < 0.001$) after treatment for 12 week **(Table 1)**.

There was statistically significant increase in HDL (49.76 ± 5.04 *vs*. 45.48 ± 7.26, $P < 0.05$) levels in rosuvastatin group when compared with atorvastatin after therapy. However, the reductions in serum cholesterol, triglyceride, LDL, and VLDL showed no statistically significant difference in both the groups ($P > 0.05$) **(Table 2)**.

Rosuvastatin reduced LDL levels by 44.25%, atorvastatin reduced LDL levels by 35.56%, . Rosuvastatin showed 30.83% reduction in cholesterol levels while atorvastatin reduced

cholesterol levels by 25.75. The HDL levels were increased by 18.31 and 7.11 in the rosuvastatin and atorvastatin groups respectively **(Table 3)**.

Table 1: Comparative Effect of Rosuvastatin and Atorvastatin on Lipid Profile Parameter Before and After Therapy

Lipid Profile Parameter (mgs %)	Rosuvastatin Mean ± SD		Atorvastatin Mean ± SD	
	Before	After	Before	After
Serum Cholesterol	284.38 ± 50.81**	196.71 ± 32.57**	270.86 ± 43.32**	201.11 ± 33.38**
Serum Triglyceride	245.46 ± 32.42**	196.06 ± 26.94*	255.41 ± 45.13**	221.84 ± 77.00**
HDL	42.06 ± 3.30**	49.76 ± 5.04**	42.46 ± 7.71**	45.48 ± 7.26**
LDL	193.23 ± 50.28**	107.73 ± 32.87**	177.34 ± 46.29**	114.27 ± 35.85**
VLDL	49.09 ± 6.48**	39.21 ± 5.39**	51.05 ± 9.03**	41.37 ± 8.24**

HDL: High-density lipoproteins, LDL: Low density lipoproteins, VLDL: Very low density lipoproteins; **'*P*' <0.001 (Highly statistically significant); *'*P*'< 0.05 (Statistically significant)

Table 2: Comparative Effect of Rosuvastatin and Atorvastatin on Lipid Profile Parameter After Therapy

Lipid profile parameter (mgs %)	After rosuvastatin therapy Mean ± SD	After atorvastatin therapy Mean ± SD	'*P*' value
Serum cholesterol	196.71 ± 32.57	201.11 ± 33.38	> 0.05
Serum triglyceride	196.06 ± 26.94	221.84 ± 77.00	> 0.05
HDL	49.76 ± 5.04	45.48 ± 7.26	< 0.05*
LDL	107.73 ± 32.87	114.27 ± 35.85	> 0.05
VLDL	39.21 ± 5.39	41.37 ± 8.24	> 0.05

HDL: High-density lipoproteins; LDL: Low density lipoproteins; VLDL: Very low density lipoproteins; *'*P*' < 0.05 (Statistically significant)

Table 3: Percentage Changes on the Various Parameters of Lipid Profile After Administration of Rosuvastatin and Atorvastatin

Lipid profile parameter (mgs %)	Rosuvastatin group (%)	Atorvastatin group (%)
Serum cholesterol	↓ 30.83	↓ 25.75
Serum triglyceride	↓ 20.13	↓ 13.14
HDL	↑ 18.31	↑ 7.11
LDL	↓ 44.25	↓ 35.56
VLDL	↓ 20.13	↓ 18.96

HDL: High-density lipoproteins; LDL: Low density lipoproteins; VLDL: Very low density lipoproteins

Safety

No clinically significant adverse events were observed in any of the study groups. Both rosuvastatin and atorvastatin groups did not deviate significantly from their baseline biochemical profile after 12 weeks of therapy. Particular attention focused on the presence of myopathy or elevated serum transaminase levels because these conditions have been associated with the use of reductase inhibitors.

DISCUSSION

In the present study, total 40 patients of dyslipidemia were divided into two groups of 20 each out of which one group received rosuvastatin 10 mg and the other group received atorvastatin10 mg for 12 weeks. The criteria for evaluation were lipid profile parameters, namely, serum cholesterol, serum triglyceride, LDL, VLDL, and HDL.

Rosuvastatin decreased the levels of serum cholesterol, serum triglyceride, LDL, VLDL and increased the levels of HDL after therapy for 12 weeks. The difference in the studied lipid parameters after therapy was highly statistically significant ($P < 0.001$). These results are in accordance with the pilot study with rosuvastatin conducted by Gleuck *et al*, at The Cholesterol Centre, Jewish Hospital, Cincinnati, USA **[13].**

Atorvastatin also decreased the levels of serum cholesterol, serum triglyceride, LDL, VLDL and increased the levels of HDL after therapy for 12 weeks. The difference in the studied lipid parameters after therapy in both the drug groups was highly statistically significant ($P < 0.001$). These results are in accordance with the studies conducted by Goudevenos *et al* **[14]** and Lewin *et al*, **[15]** for the efficacy of atorvastatin in dyslipidemia.

When the LDL level reduction in rosuvastatin group with that of atorvastatin group was compared, it was observed that the reduction in LDL levels in rosuvastatin group were statistically nonsignificant when compared with atorvastatin group. These results are in contrast to a study conducted by Bullano *et al*, which concluded that rosuvastatin was more effective than atorvastatin in reducing LDL levels significantly **[16]**.

The rise in HDL levels in rosuvastatin group after therapy was statistically significant when compared with atorvastatin group . In contrast to this, the use of rosuvastatin *vs* atorvastatin in type 2 diabetes mellitus (URANUS) study group found that both rosuvastatin and atorvastatin increased HDL-C and decreased TG from baseline to 4 weeks, but there were no statistically significant differences between the groups **[17]**. The COMETS study (a comparative study with rosuvastatin in subjects with metabolic syndrome) concluded that rosuvastatin increased high-density lipoprotein cholesterol significantly more than atorvastatin **[18]**.

The comparison of the serum cholesterol reduction in rosuvastatin group with that of atorvastatin group revealed that the reduction in serum cholesterol levels in rosuvastatin

group were statistically nonsignificant when compared with atorvastatin group.

The intergroup comparison of reduction of serum triglycerides and VLDL after therapy among the rosuvastatin and atorvastatin groups was statistically nonsignificant (P>0.05).

Rosuvastatin reduced LDL levels by 44.25%, while atorvastatin reduced LDL levels by 35.56%. These results are consistent with the STELLAR trial where rosuvastatin and atorvastatin reduced LDL levels by 45.8 and 36.8 respectively **[19]**.

CONCLUSION

In summary, 10 mg of rosuvastatin tablet was comparable to 10 mg of atorvastatin tablet in reducing LDL levels after 12 weeks of therapy in patients of dyslipidemia. Also, 10 mg of rosuvastatin was more efficacious than 10 mg of both atorvastatin in increasing HDL levels after 12 weeks of therapy in patients of dyslipidemia. No adverse events were noted with both the statins used. However, further studies are necessary to conclusively prove the efficacy of rosuvastatin over the existing statins.

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